Development of Tolerant and Other Complex Phenotypes for Biofuel Production

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In bioprocessing, in addition to maximizing the flux for a desirable product, the robustness and prolonged productivity of the biocatalyst (the cells) under realistic bioprocessing conditions is an equally important issue. Thus, the ability of cells to withstand "stressful- bioprocessing conditions without loss of productivity is a most significant goal. Such conditions include: toxic substrates, accumulation of toxic products and byproducts, high or low pH, or high salt concentrations as encountered in most applications for the production of chemicals and biofuels as well as in bioremediation applications. The difficulty—but also the intellectual and biotechnological challenge—is that the desirable phenotypic trait is determined by several genes or a complex regulatory circuit. Complex phenotypes are also encountered when one desires to develop a *de novo* capability or pathway in a particular cell type. For example, how do cells put together the regulatory elements of a sequence of genes to make a pathway or program possible? Yes, it is an evolutionary process, but if we are to "imitate" the process, what would we do? What tools could one possibly use and strategies to facilitate the development of complex phenotypes in microbial cells? From omics-based analysis to synthesis, all selection based, or hybrid? Knowledge-based and mechanistic or not? This will be the focus of this presentation, together with some data from early efforts to demonstrate some key concepts that we explore in my laboratory.